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L1: Entry 8 of 20

File: USPT

Dec 26, 2000

DOCUMENT-IDENTIFIER: US 6165713 A

TITLE: Composition and methods relating to DNA mismatch repair genes

Other Reference Publication (40):

Sean Baker et al., "Male Mice Defective in the DNA Mismatch Repair Gene PMS2 Exhibit Abnormal Chromosome Synapsis in Meiosis," Cell, Jul. 28, 1995, vol. 82, No. 2, pp. 309-319.

**WEST****End of Result Set**

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L3: Entry 1 of 1

File: USPT

Nov 14, 2000

US-PAT-NO: 6146894

DOCUMENT-IDENTIFIER: US 6146894 A

TITLE: Method for generating hypermutable organisms

DATE-ISSUED: November 14, 2000

## INVENTOR-INFORMATION

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US-CL-CURRENT: 435/440; 435/325, 435/455

## CLAIMS:

We claim:

1. A method of making a mammalian hypermutable cell, comprising the step of: introducing into a mammalian cell a polynucleotide comprising a dominant negative allele of the mismatch repair gene, PMS2, whereby the cell becomes hypermutable.
2. The method of claim 1 wherein the polynucleotide is introduced by transfection of a suspension of cells in vitro.
3. The method of claim 1 wherein the mismatch repair gene is human PMS2.
4. The method of claim 3 wherein the allele comprises a truncation mutation.
5. The method of claim 3 wherein the allele comprises a truncation mutation at codon 134 as shown in SEQ ID NO: 1.
6. The method of claim 5 wherein the truncation mutation is a thymidine at nucleotide 424 of wild-type PMS2 as shown in SEQ ID NO: 1.
7. A homogeneous composition of cultured, hypermutable, mammalian cells which comprise a dominant negative allele of the mismatch repair gene, PMS2.
8. The homogenous composition of claim 7 wherein the mismatch repair gene is human PMS2.
9. The homogeneous composition of claim 7 wherein the cells express a protein consisting of the first 133 amino acids of human PMS2 which functions as a dominant-negative protein.
10. The homogeneous composition of claim 7 wherein the cells express a protein consisting of the first 133 amino acids of PMS2 which functions as a dominant-negative protein.
11. A method of generating a mutation in a gene of interest comprising the steps of: growing a population of mammalian cells comprising the gene of interest and a dominant negative allele of the mismatch repair gene PMS2, wherein the cell is hypermutable; identifying a cell wherein the gene of interest harbors a mutation.

12. The method of claim 11 wherein the step of identifying comprises analyzing a nucleotide sequence of the gene of interest.
13. The method of claim 11 wherein the step of identifying comprises analyzing mRNA transcribed from the gene of interest.
14. The method of claim 11 wherein the step of identifying comprises analyzing a protein encoded by the gene of interest.
15. The method of claim 11 wherein the step of identifying comprises analyzing the phenotype of the gene of interest.
16. The method of claim 11 wherein the mammalian cells are made by the process of introducing a polynucleotide comprising a dominant negative allele of a mismatch repair gene into a mammalian cell, whereby the cell becomes hypermutable.
17. The method of claim 16 wherein the mismatch repair gene encodes a truncated PMS2.
18. The method of claim 16 wherein the mismatch repair gene encodes a truncated human PMS2.
19. The method of claim 15 wherein the step of identifying comprises analyzing a nucleotide sequence of the gene of interest.
20. The method of claim 15 wherein the step of identifying comprises analyzing mRNA transcribed from the gene of interest.
21. The method of claim 15 wherein the step of identifying comprises analyzing a protein encoded by the gene of interest.
22. The method of claim 15 wherein the step of identifying comprises analyzing the phenotype of the gene of interest.

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